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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,364	11/14/2001	Johann Engelhardt	2203/50472	6798

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EXAMINER

GEISEL, KARA E

ART UNIT PAPER NUMBER

2877

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

EV

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/987,364	ENGELHARDT, JOHANN	
	Examiner	Art Unit	
	Kara E. Geisel	2877	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 January 2005.  
 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3, 5-13 and 15-19 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☒ Claim(s) 1-3 and 5-8 is/are allowed.  
 6) ☒ Claim(s) 9-13 and 15-19 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☒ The drawing(s) filed on 05 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All b) ☐ Some \* c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                            | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

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## DETAILED ACTION

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9-13, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Müller (USPN 5,978,083) in view of Baer (USPN 5,866,911).

In regards to claims 9 and 15, Müller discloses an apparatus for measuring the properties of an excited state in a specimen (fig. 1), wherein the apparatus comprises an electromagnetic energy source (1) that emits light of one wavelength, a means for dividing the light into at least a first and a second partial light beam (4) and an intermediate element in at least one partial light beam to influence the time of travel of the at least one partial light beam (5). It is not specifically disclosed that the properties measured is the lifetime of the excited state in a specimen, however, it is disclosed that the measurement of the properties can be made over a time period in order to produce time-resolved measurements (column 7, lines 62-65). The examiner takes Official Notice that it is well known in the art that lifetime measurements are useful in determining the identity of a fluorophore that is being excited to fluoresce, especially if there are multiple fluorophores in a solution that can be excited by the same wavelength but have different lifetimes (see prior art). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use this method to make lifetime measurements, since it can be used to take measurements over time, in order to identify a fluorophore in a solution of multiple fluorophores that are excited by the same wavelength but have different lifetimes. Müller does not disclose that an element for wavelength modification, such as an element for frequency multiplication, is provided in one partial

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light beam. However, it is disclosed that it would be possible to configure the apparatus in order to have the wavelengths of the partial light beams be different (column 10, lines 22-31). This would be done to allow different multi-photon excitations to occur, allowing more flexibility in the types of fluorescent substances used, while still only using one laser and saving on the cost of multiple, different wavelength lasers.

Baer generally teaches placing an element for frequency multiplication in the path of a light beam in order to change the wavelength of that light beam (column 11, lines 52-54). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to place the element for frequency multiplication of Baer's apparatus into the path of one of the partial light beams of Müller's apparatus, so that the wavelength of that light beam can be changed, in order to allow more flexibility in the types of fluorescent substances used, while still only using one laser to produce the beams.

In regards to claims 10-11, the first partial light beam is an exciting light beam directed onto a specimen, and excites a defined subregion there and the second partial light beam defines an emitting light beam and is directed onto the specimen in such a way that the subregion of the specimen is at least partially overlapped (Müller columns 7-8, lines 45-67 and 1-19, respectively).

In regards to claim 12, the intermediate element modifies the length of the optical light path (Müller column 6, lines 42-47).

In regards to claim 13, the intermediate element is configured movably and thereby defines a chicane having an adjustable passage length (Müller column 6, lines 42-47).

In regards to claim 16, the excitation can be multi-photon excitation (Müller column 7, lines 59-62).

In regards to claims 17-18, the electromagnetic energy can be a pulsed laser (Müller column 3, lines 21-23).

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In regards to claim 19, Müller discloses a scanning microscope comprising a device for generating a relative motion between an illuminating light beam and a specimen (column 9, lines 22-24), a microscope optical system (fig. 1), a detector (11), and an apparatus for measuring the properties of an excited state in a specimen (10). Furthermore, the apparatus for measuring the lifetimes of an excited state in a specimen has an electromagnetic energy source that emits light of one wavelength (1), a means for dividing the light into at least a first and a second partial light beam (4), and an intermediate element in at least one partial light beam to influence the time of travel of the at least one partial light beam (5). It is not specifically disclosed that the properties measured is the lifetime of the excited state in a specimen, however, it is disclosed that the measurement of the properties can be made over a time period in order to produce time-resolved measurements (column 7, lines 62-65). The examiner takes Official Notice that it is well known in the art that lifetime measurements are useful in determining the identity of a fluorophore that is being excited to fluoresce, especially if there are multiple fluorophores in a solution that can be excited by the same wavelength but have different lifetimes (see prior art). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use this method to make lifetime measurements, since it can be used to take measurements over time, in order to identify a fluorophore in a solution of multiple fluorophores that are excited by the same wavelength but have different lifetimes. Müller does not disclose that an element for wavelength modification, such as an element for frequency multiplication, is provided in one partial light beam. However, it is disclosed that it would be possible to configure the apparatus in order to have the wavelengths of the partial light beams be different (column 10, lines 22-31). This would be done to allow different multi-photon excitations to occur, allowing more flexibility in the types of fluorescent substances used, while still only using one laser and saving on the cost of multiple, different wavelength lasers.

Baer generally teaches placing an element for frequency multiplication in the path of a light beam in order to change the wavelength of that light beam (column 11, lines 52-54). Therefore, it would have

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been obvious to one of ordinary skill in the art at the time the invention was made to place the element for frequency multiplication of Baer's apparatus into the path of one of the partial light beams of Müller's apparatus, so that the wavelength of that light beam can be changed, in order to allow more flexibility in the types of fluorescent substances used, while still only using one laser to produce the beams.

Claims 9-13, and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pope et al. (USPN 5,308,971) in view of Baer (USPN 5,866,911).

In regards to claims 9 and 15, Pope discloses an apparatus for measuring the lifetime of an excited state in a specimen (fig. 1, 10), wherein the apparatus comprises an electromagnetic energy source (11) that emits light of one wavelength (column 3, lines 44-50), a means for dividing the light into at least a first and a second partial light beam (13) and an intermediate element in at least one partial light beam to influence the time of travel of the at least one partial light beam (20-21). Pope does not disclose that an element for wavelength modification, such as an element for frequency multiplication, is provided in one partial light beam. However, it is disclosed that this apparatus is used so that the generated exciting and emitting wavelengths are the same (column 4, lines 1-2), but that it would be possible to configure the apparatus in order to have the exciting and emitting wavelengths be different (column 4, lines 2-4, i.e. changing the wavelength of one partial light beam). This would be done to allow different multi-photon excitations to occur, allowing more flexibility in the types of fluorescent substances used.

Baer generally teaches placing an element for frequency multiplication in the path of a light beam in order to change the wavelength of that light beam (column 11, lines 52-54). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to place the element for frequency multiplication of Baer's apparatus into the path of one of the partial light beams of Pope's apparatus, so that the wavelength of that light beam can be changed, in order to allow more flexibility in the types of fluorescent substances used.

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In regards to claim 10, the first partial light beam is an exciting light beam directed onto a specimen (30), and excites a defined subregion there (Pope column 4, lines 33-38).

In regards to claim 11, the second partial light beam defines an emitting light beam and is directed onto the specimen in such a way that the subregion of the specimen is at least partially overlapping (Pope column 4, lines 38-47).

In regards to claim 12, the intermediate element modifies the length of the optical light path (Pope column 3, lines 58-66).

In regards to claim 13, the intermediate element is configured movably and thereby defines a chicane having an adjustable passage length (Pope column 3, lines 58-66).

In regards to claim 16, the excitation can be multi-photon excitation (Pope columns 5-6, lines 62-68 and 1-2, respectively).

In regards to claims 17-18, the electromagnetic energy is a pulsed laser (Pope column 3, lines 44-50).

#### *Allowable Subject Matter*

Claims 1-3, and 5-8 are allowed over the prior art of record for the reasons set forth in the previous Office Action (paper number 0904).

#### *Response to Arguments*

Applicant's arguments filed January 5<sup>th</sup>, 2005, on pages 11-12, with regards to the rejection of claims 9-20 have been fully considered but they are not persuasive. Specifically, applicant argues that there would be no motivation to combine Pope with Müller since they are non-analogous art and that it is hindsight reasoning. The Examiner does not agree. Pope's apparatus is in the same field of endeavor as Baer's in that they both are concerned with measuring the fluorescence from a sample being excited, and that they both excite the sample using a laser beam. Pope discloses that partial light beams in the invention used to excite the sample are of the same wavelength, but it would be possible to arrange the

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apparatus so that the partial light beams are of different wavelengths (column 4, lines 1-5). This would be done in order to excite samples, using multi-photon excitation, that require photons of different wavelengths to be excited. This gives motivation for one of ordinary skill in the art to look for ways to change the wavelength of one of the partial light beams. Baer discloses a device in the same field of endeavor as Pope's, which has a means for changing the wavelength of a beam of light (column 11, lines 49-55). One of ordinary skill in the art would have been motivated to combine Baer's means of changing the wavelength of a beam of light with Pope's device, by placing the means of changing the wavelength of a beam of light into one of the partial light beams so that the partial beams could be of different wavelengths, and so that the fluorescence of a sample that needs photons of different wavelengths to be excited, via multi-photon excitation, could be measured.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Therefore, the rejection of these claims has been maintained.

#### *Additional Prior Art*

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The prior art made of record is Gombrich et al. (USPN 6,081,740), and Jensen et al. (USPN 6,447,724).

Gombrich generally discloses using time-resolved measurements to measure the lifetimes of different fluorophores, in order to identify the fluorophore.

Jensen generally discloses identifying fluorescent samples by measuring their characteristic fluorescence lifetime.



*Conclusion*

Several facts have been relied upon from the personal knowledge of the examiner about which the examiner took Official Notice. Applicant must seasonably challenge well known statements and statements based on personal knowledge when they are made by the Board of Patent Appeals and Interferences. In re Selmi, 156 F.2d 96, 70 USPQ 197 (CCPA 1946); In re Fischer, 125 F.2d 725, 52 USPQ 473 (CCPA 1942). See also In re Boon, 439 F.2d 724, 169 USPQ 231 (CCPA 1971) (a challenge to the taking of judicial notice must contain adequate information or argument to create on its face a reasonable doubt regarding the circumstances justifying the judicial notice). If applicant does not seasonably traverse the well-known statement during examination, then the object of the well-known statement is taken to be admitted prior art. In re Chevenard, 139 F.2d 71, 60 USPQ 239 (CCPA 1943). A seasonable challenge constitutes a demand for evidence made as soon as practicable during prosecution. Thus, applicant is charged with rebutting the well-known statement in the next reply after the Office action in which the well-known statement was made.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kara E Geisel whose telephone number is **571 272 2416**. The examiner can normally be reached on Monday through Friday, 8am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gregory J. Toatley, Jr. can be reached on **571 272 2800 ext. 77**. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872 9306 for regular communications and 703 872 9306 for After Final communications.



F.L. Evans  
Primary Examiner  
Art Unit 2877

*K.G.*  
KEG  
March 19, 2005